Freeform Search

Database: US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Term: 19 and L12

Display: 20 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ **Hit List** ◉ **Hit Count** ○ **Side by Side** ○ **Image**

Search Clear Interrupt

Search History

DATE: Thursday, December 18, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT; PLUR=YES; OP=AND			
L14	toxicity and L13	5	L14
L13	l9 and L12	17	L13
L12	(hepatic or renal) near3 toxin or neurotoxin or myotoxin or carcinogen or cosmetics or agricultural adj (chemical or agent) or teratogen$	67726	L12
L11	toxicity and l9	13	L11
L10	l5 and L9	3	L10
L9	l1 with L8	85	L9
L8	molecular near5 profile or (gene or protein) near5 (expression near3 pattern)	8678	L8
L7	l1 near10 l5	0	L7
L6	l4 and L5	555	L6
L5	troglitazone or erythromycin	8752	L5
L4	toxicity and l3	6750	L4
L3	l1 and L2	18559	L3
L2	molecular near5 profile or (gene or protein) near5 (expression or pattern)	67087	L2
L1	embryo or rmbryoid adj bod$ or fetus	27387	L1

h e b b g e e e e hee b f ff e ch

Generate Collection | Print

Search Results - Record(s) 1 through 17 of 17 returned.

☐ 1. 20030207853. 20 May 03. 06 Nov 03. Cholesterol and hedgehog signaling. Beachy, Philip A., et al. 514/176; 514/1 A61K031/58 A61K031/00.

☐ 2. 20030203885. 19 May 03. 30 Oct 03. Cholesterol and hedgehog signaling. Beachy, Philip A., et al. 514/176; A61K031/58.

☐ 3. 20030148510. 15 Jan 02. 07 Aug 03. Methods of inducing differentiation in stem cells, methods of generating tissue using scaffold matrices derived from micro-organs and stem cells, methods of producing adult stem cells and methods of continuously generating stem cells by implantation of micro-organs as sources of stem cells. Mitrani, Eduardo N.. 435/325; 435/366 C12N005/08.

☐ 4. 20030134413. 03 Dec 02. 17 Jul 03. Cell production. Rathjen, Peter David, et al. 435/368; C12N005/08.

☐ 5. 20030115637. 23 Oct 02. 19 Jun 03. Embryo sac-specific genes. Dresselhaus, Thomas, et al. 800/287; 435/183 435/320.1 435/419 435/6 530/370 536/23.6 800/279 A01H001/00 C12N009/00 C12N015/82 C12Q001/68 C07H021/04 C12P021/02 C07K014/415 C12N005/04.

☐ 6. 20030028909. 13 May 02. 06 Feb 03. Transgenic zebra fish embryo model for hematopoiesis and lymphoproliferative disorders. Uckun, Fatih M., et al. 800/10; 435/7.23 A01K067/00 G01N033/574.

☐ 7. 20020164682. 03 Jun 98. 07 Nov 02. MAMMALIAN CERBERUS-LIKE PROTEIN AND COMPOSITIONS. FOLLETTIE, MAXIMILLIAN, et al. 435/69.1; 424/130.1 435/320.1 435/325 514/12 530/350 536/23.5 C12P021/06 A61K038/00 A61K039/395 C07K017/00 C07K001/00 C12N015/74 C12N015/63 C12N015/00 C12N015/09 C12N015/70 C12N005/00 C07K014/00 C12N005/02 C07H021/04.

☐ 8. 20020102604. 07 Dec 00. 01 Aug 02. Full-length human cDNAs encoding potentially secreted proteins. Milne Edwards, Jean-Baptiste Dumas, et al. 435/7.1; 530/350 536/23.1 G01N033/53 C07H021/02 C07H021/04 C07K001/00 C07K014/00 C07K017/00.

☐ 9. 20020045607. 11 Sep 01. 18 Apr 02. Cholesterol and hedgehog signaling. Beachy, Philip A., et al. 514/176; A61K031/58.

☑ 10. 20020025297. 05 Sep 01. 28 Feb 02. Methods of screening agents for activity using teleosts. Serbedzija, George N., et al. 424/9.2; 800/20 800/3 A61K049/00 A01K067/027.

☐ 11. 6656449. 23 Aug 00; 02 Dec 03. Methods of screening agents for activity using teleosts. Serbedzija; George, et al. 424/9.2; 424/9.1 424/9.34 424/9.6. A61K049/00 A61B005/055 A61B010/00.

☐ 12. 6299858. 22 Feb 99; 09 Oct 01. Methods of screening agents for activity using teleosts. Serbedzija; George N., et al. 424/9.2; 424/9.1 424/9.6. A61K049/00 A61B005/055 A61B010/00.

☐ 13. 6288048. 12 Feb 99; 11 Sep 01. Cholesterol and hedgehog signaling. Beachy; Philip A., et al.

h e b b g e e e f e e e e hee b ch

514/176; 435/962 436/63 436/71 436/86 436/87 436/92 514/278. A61K031/58.

☐ 14. 6262025. 07 Apr 98; 17 Jul 01. Nucleotide and protein sequences of vertebrate delta genes and methods based thereon. Ish-Horowicz; David, et al. 514/12; 530/300 530/350. C07K014/00.

☐ 15. 6004924. 06 Mar 96; 21 Dec 99. Protein sequences of serrate gene products. Ish-Horowicz; David, et al. 514/2; 514/13 514/15 530/300 530/326 530/328 530/350. A01N037/18 A61K037/00 C07K014/00.

☐ 16. 5935852. 03 Jul 97; 10 Aug 99. DNA molecules encoding mammalian cerberus-like proteins. Follettie; Maximillian, et al. 435/325; 435/252.3 435/252.33 435/254.11 435/320.1 435/357 435/358 435/366 536/23.1 536/23.5 536/24.31. C12N015/11 C12N015/85 C12N001/21 C07H021/04.

☐ 17. 5869282. 07 Mar 95; 09 Feb 99. Nucleotide and protein sequences of the serrate gene and methods based thereon. Ish-Horowicz; David, et al. 435/69.1; 435/252.3 435/320.1 435/325 530/300 530/350 536/23.1 536/24.3. C12P021/00 C12N015/00 C07H017/00 C07K014/00.

Generate Collection Print

Terms	Documents
L9 and L12	17

Prev Page Next Page Go to Doc#

h e b b g e e e f e e e e hee b ch

Freeform Search

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: toxicity and l9

Display: 20 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search Clear Interrupt

Search History

DATE: Thursday, December 18, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT; PLUR=YES; OP=AND			
L11	toxicity and l9	13	L11
L10	l5 and L9	3	L10
L9	l1 with L8	85	L9
L8	molecular near5 profile or (gene or protein) near5 (expression near3 pattern)	8678	L8
L7	l1 near10 l5	0	L7
L6	l4 and L5	555	L6
L5	troglitazone or erythromycin	8752	L5
L4	toxicity and l3	6750	L4
L3	l1 and L2	18559	L3
L2	molecular near5 profile or (gene or protein) near5 (expression or pattern)	67087	L2
L1	embryo or rmbryoid adj bod$ or fetus	27387	L1

END OF SEARCH HISTORY

h e b b g e e e e hee b f ff e ch

Generate Collection Print

Search Results - Record(s) 1 through 13 of 13 returned.

☐ 1. 20030148510. 15 Jan 02. 07 Aug 03. Methods of inducing differentiation in stem cells, methods of generating tissue using scaffold matrices derived from micro-organs and stem cells, methods of producing adult stem cells and methods of continuously generating stem cells by implantation of micro-organs as sources of stem cells. Mitrani, Eduardo N.. 435/325; 435/366 C12N005/08.

☐ 2. 20030140372. 19 Aug 02. 24 Jul 03. Genes for desaturases to alter lipid profiles in corn. Shen, Jennie Bih-Jien. 800/281; 435/190 435/320.1 435/419 435/69.1 536/23.2 800/320.1 A01H005/00 C12N015/82 C07H021/04 C12N009/04 C12P021/02 C12N005/04.

☐ 3. 20030027783. 17 May 02. 06 Feb 03. Inhibiting gene expression with dsRNA. Zernicka-Goetz, Magdalena, et al. 514/44; 424/93.2 435/6 A61K048/00 C12Q001/68.

☐ 4. 20030017549. 24 Jan 02. 23 Jan 03. Methods and compositions for expressing polynucleotides specifically in smooth muscle cells in vivo. Owens, Gary K., et al. 435/69.7; 435/183 435/320.1 435/325 530/350 530/351 536/23.5 C12P021/02 C12N005/06 C07H021/04 C12N009/00 C07K014/52.

☐ 5. 20020114784. 04 Jan 02. 22 Aug 02. Composition and method for in vivo and in vitro attenuation of gene expression using double stranded RNA. Li, Yin-Xiong, et al. 424/93.2; 435/455 435/456 A61K048/00 C12N015/86.

☐ 6. 20020102724. 17 Aug 01. 01 Aug 02. Novel hematopoietic genes and polypeptides. Hidaka, Michihiro, et al. 435/320.1; 424/130.1 435/419 435/6 435/69.1 435/7.1 435/7.4 530/350 536/23.6 536/24.1 536/24.3 800/13 800/278 C12Q001/68 G01N033/573 C07H021/04 C12P021/06 C12N015/82 C12N015/09 C12N015/29 C07K001/00 C07K014/00 C12N005/04 C07K016/00.

☐ 7. 20020102604. 07 Dec 00. 01 Aug 02. Full-length human cDNAs encoding potentially secreted proteins. Milne Edwards, Jean-Baptiste Dumas, et al. 435/7.1; 530/350 536/23.1 G01N033/53 C07H021/02 C07H021/04 C07K001/00 C07K014/00 C07K017/00.

☐ 8. 20020025297. 05 Sep 01. 28 Feb 02. Methods of screening agents for activity using teleosts. Serbedzija, George N., et al. 424/9.2; 800/20 800/3 A61K049/00 A01K067/027.

☐ 9. 6656449. 23 Aug 00; 02 Dec 03. Methods of screening agents for activity using teleosts. Serbedzija; George, et al. 424/9.2; 424/9.1 424/9.34 424/9.6. A61K049/00 A61B005/055 A61B010/00.

☑ 10. 6586217. 18 Dec 98; 01 Jul 03. Mammalian selenophosphate synthetase. Guimaraes; M. Jorge, et al. 435/194; 435/183 435/252.3 435/325 435/6 435/69.1 435/91.2 514/44 536/23.1 536/23.2 536/24.3 536/24.31 536/24.33. C12N015/12 C12N015/54 C12N009/12.

☐ 11. 6548290. 11 Jun 98; 15 Apr 03. Geminin gene and protein. McGarry; Thomas J., et al. 435/252.3; 435/320.1 435/325 536/23.2 536/23.5. C12N015/00.

☑ 12. 6299858. 22 Feb 99; 09 Oct 01. Methods of screening agents for activity using teleosts. Serbedzija; George N., et al. 424/9.2; 424/9.1 424/9.6. A61K049/00 A61B005/055 A61B010/00.

h e b b g e e e f e e e e hee b ch

☐ 13. 6060590. 31 Mar 98; 09 May 00. Chitinase related proteins and methods of use. Bryant; Peter J., et al. 530/399; 530/350. C07K014/435 C07K014/475.

Generate Collection Print

Terms	Documents
toxicity and L9	13

Prev Page Next Page Go to Doc#

h e b b g e e e f e e e e hee b ch

Generate Collection Print

Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. 20030073637. 01 Oct 02. 17 Apr 03. Method for stimulating connective tissue growth or wound healing. Uutela, Marko, et al. 514/12; 435/320.1 435/455 514/44 A61K048/00 A61K038/18 C12N015/85.

☐ 2. 20020164710. 04 Mar 02. 07 Nov 02. Platelet-derived growth factor D, DNA coding therefor, and uses thereof. Eriksson, Ulf, et al. 435/69.1; 435/320.1 435/325 530/350 530/399 536/23.5 C07K014/49 C07H021/04 C12P021/02 C12N005/06.

☐ 3. 20020136726. 20 Nov 01. 26 Sep 02. Artery smooth muscle- and vein smooth muscle-specific proteins and uses therefor. Anderson, David J., et al. 424/146.1; A61K039/395.

Generate Collection Print

Terms	Documents
L5 and L9	3

Prev Page Next Page Go to Doc#

h e b b g e e e f e e e e hee b ch

=> d his

(FILE 'HOME' ENTERED AT 14:29:41 ON 18 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:31:13 ON 18 DEC 2003

```
L1       784358 S EMBRYO OR EMBRYOID(W)BOD? OR FETUS
L2         7391 S MOLECULAR(5A)PROFILE
L3      1292275 S (GENE OR PROTEIN)(5A)(EXPRESSION OR PATTERN)
L4      1298727 S L2 OR L3
L5        86336 S L1 AND L4
L6      1008534 S TOXICITY
L7          910 S L5 AND L6
L8        61066 S TROGLITAZONE OR ERYTHROMYCIN
L9            1 S L7 AND L8
L10       53347 S (HEPATIC OR RENAL)(3A)TOXIN OR NEUROTOXIN OR MYOTOXIN
L11      407061 S TERATOGENIC OR CARCINOGEN OR COSMETICS OR AGRICULTUR?(3A)(CHE
L12          24 S L7 AND L10
L13         159 S L7 AND L11
L14          24 DUP REM L12 (0 DUPLICATES REMOVED)
L15         116 DUP REM L13 (43 DUPLICATES REMOVED)
```

=> d bib ab 19

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:402043 CAPLUS
DN 133:26835
TI **Toxicity** typing using **embryoid bodies**
IN Snodgrass, H. Ralph
PA Vistagen, Inc., USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000034525	A1	20000615	WO 1999-US29384	19991209
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1137809	A1	20011004	EP 1999-963069	19991209
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002531852	T2	20020924	JP 2000-586957	19991209
	US 2001039006	A1	20011108	US 2001-864621	20010523
PRAI	US 1998-111640P	P	19981209		
	US 1999-457931	A	19991208		
	WO 1999-US29384	W	19991209		

AB This invention provides methods and systems for identifying and typing **toxicity** of chem. compns., as well as for screening new compns. for **toxicity**. The invention involves detecting alterations in **gene** or **protein expression** and hence establishing **mol. profiles** in isolated mammalian **embryoid bodies** contacted with various chem. compns. of known and unknown **toxicities**, and correlating the **mol. profiles** with **toxicities** of the chem. compns.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 1-24 au ti so ab l14

L14 ANSWER 1 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Perrone-Bizzozero, N. I. [Reprint Author]; Yang, Y. [Reprint Author]; Caldeira, J. [Reprint Author]; Caldwell, K. K. [Reprint Author]; Valenzuela, C. F. [Reprint Author]; Savage, D. D. [Reprint Author]
TI Fetal alcohol exposure alters the **expression** of several plasticity-associated **genes** in the hippocampus of adult rat offspring.
SO Alcoholism Clinical and Experimental Research, (May 2003) Vol. 27, No. 5 Supplement, pp. 124A. print.
Meeting Info.: Scientific Meeting of the Research Society on Alcoholism and the 12th Congress of the International Society for Biomedical Research on Alcoholism. Fort Lauderdale, FL, USA. June 21-25, 2003. Research Society on Alcoholism; International Society for Biomedical Research on Alcoholism.
CODEN: ACRSDM. ISSN: 0145-6008.

L14 ANSWER 2 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Brambila, Eduardo; Liu, Jie; Morgan, Daniel L.; Beliles, Robert P.; Waalkes, Michael P. [Reprint author]
TI Effect of mercury vapor exposure on metallothionein and glutathione S-transferase **gene expression** in the kidney of nonpregnant, pregnant, and neonatal rats.
SO Journal of Toxicology and Environmental Health Part A, (September 13, 2002) Vol. 65, No. 17, pp. 1273-1288. print.
ISSN: 1528-7394.
AB Elemental mercury (Hg0) is a ubiquitous toxic pollutant. Exposure to Hg0 vapor typically is by inhalation, and the kidney is the primary target organ. Glutathione (GSH) and metallothionein (MT) appear to mitigate mercury **toxicity**. However, little is known about GSH or MT regulation after Hg0 vapor exposure, particularly during pregnancy, a time of high sensitivity to most metals. Thus, this study sought to determine renal mercury accumulation and MT- and GSH-related **gene expression** following Hg0 vapor exposure in nonpregnant, pregnant, and neonatal rats exposed in utero. Groups (n=5) of pregnant rats (Long-Evans) were exposed to Hg0 vapor (4 mg/m3) or air (control) for 2 h/d from gestational day (GD) 6 to 15, and kidneys from dams and pups were removed at various times during and after the onset of exposure. For comparative purposes, nonpregnant female rats were exposed to Hg0 for 10 d under the same conditions. Renal mercury, MT protein, and GST activity were assayed by standard analytical techniques. Western blot analysis was also performed using antibodies against MT and GST-pi. GSH-related **gene expression** was studied by cDNA microarray. Hg0 vapor exposure produced renal accumulation of mercury in nonpregnant, pregnant, and neonatal rats. However, the transplacentally exposed neonates accumulated approximately 1000-fold less mercury than adults. Hg0 vapor exposure produced a time-dependent increase in renal MT protein in nonpregnant and pregnant rats, but not in neonatal rats. Maximum MT increases were observed on d 10 (fivefold) in nonpregnant and GD 15 (threefold) in pregnant rats. Activation of the MT gene by Hg0 was confirmed at the translational level by Western blot analysis and at the transcriptional level by Northern blot analysis. Microarray analysis revealed a significant upregulation in the renal expression of the GST-pi, GST-Ya, and microsomal GST and GST5-5 genes in nonpregnant and pregnant rats. Western blot and enzyme assay confirmed the upregulation of GST genes after Hg0 exposure. Thus, in response to Hg0 vapor exposure, the **expression** of the MT **gene** and various GST genes is activated in nonpregnant and pregnant rats. Activation of these genes could be part of a defensive response directed at decreasing renal mercury

toxicity, and may help divert the metal away from the **fetus**.

L14 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Storch, Alexander [Reprint author]; Lehmensiek, Vera [Reprint author]; Tan, Eva-Maria [Reprint author]; Schwarz, Johannes
TI Expression of mutant alpha-synucleins related to Parkinson's disease enhances MPP+ **toxicity** in HEK-293 cells transfected with the DAT gene.
SO Neurology, (April 9, 2002) Vol. 58, No. 7 Supplement 3, pp. A494-A495. print.
Meeting Info.: 54th Annual Meeting of the American Academy of Neurology. Denver, Colorado, USA. April 13-20, 2002.
CODEN: NEURAI. ISSN: 0028-3878.

L14 ANSWER 4 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Mengesdorf, Thorsten; Althausen, Sonja; Paschen, Wulf [Reprint author]
TI Genes associated with pro-apoptotic and protective mechanisms are affected differently on exposure of neuronal cell cultures to arsenite. No indication for endoplasmic reticulum stress despite activation of grp78 and gadd153 expression.
SO Molecular Brain Research, (15 August, 2002) Vol. 104, No. 2, pp. 227-239. print.
CODEN: MBREE4. ISSN: 0169-328X.
AB The effect of arsenite exposure on cell viability, **protein** synthesis, energy metabolism and the **expression** of **genes** coding for cytoplasmic (hsp70) and endoplasmic reticulum (ER; gadd153, grp78, grp94) stress proteins was investigated in primary neuronal cell cultures. Furthermore, signs of ER stress were evaluated by investigating xbp1 mRNA processing. Arsenite levels of 30 and 100 muM induced severe cell injury. Protein synthesis was reduced to below 20% of control in cultures exposed to 30 and 100 muM arsenite for 1 h, and it remained markedly suppressed until 24 h of exposure. Arsenite induced a transient inhibition of energy metabolism after 1 h of exposure, but energy state recovered completely after 3 h. Arsenite exposure affected the **expression** and translation of **genes** coding for HSP70 and GRP78, GRP94, GADD153 to different extents. While hsp70 mRNA levels rose drastically, approximally 550-fold after 6 h exposure, HSP70 protein levels did not change over the first 6 h. On the other hand, gadd153 mRNA levels rose only approximately 14-fold after 6 h exposure, while GADD153 protein levels were markedly increased after 3 and 6 h exposure. HSP70 protein levels were markedly increased and GADD153 protein levels decreased to almost control levels in cultures left in arsenite solution for 24 h, i.e. when only a small fraction of cells had escaped arsenite **toxicity**. Arsenite exposure of neurons thus induced an imbalance between pro-apoptotic and survival-activating pathways. Despite the marked increase in gadd153 mRNA levels, we did not observe signs of xbp1 processing in arsenite exposed cultures, indicating that arsenite did not produce ER stress.

L14 ANSWER 5 OF 24 MEDLINE on STN
AU Zheng Shuang; Chou Alice H; Jimenez Amie L; Khodadadi Omid; Son Sarah; Melega William P; Howard Bruce D
TI The fetal and neonatal brain protein neuronatin protects PC12 cells against certain types of toxic insult.
SO BRAIN RESEARCH. DEVELOPMENTAL BRAIN RESEARCH, (2002 Jun 30) 136 (2) 101-10.
Journal code: 8908639. ISSN: 0165-3806.
AB The protein neuronatin is expressed in the nervous system of the **fetus** and neonate at a much higher level than in the adult. Its function is unknown. As a result of variable splicing, neuronatin mRNA exists in two forms, alpha and beta. Wild type PC12 cells express neuronatin-alpha. We have isolated a PC12 variant, called 1.9, that retains many of the neuron-like properties of wild type PC12 cells, but it

does not express neuronatin and it exhibits markedly increased sensitivity to the toxic effects of nigericin, rotenone and valinomycin. Pretreatment of the 1.9 cells with alpha-methyltyrosine, which inhibits dopamine synthesis, had little effect on the cells' sensitivity to nigericin, rotenone or valinomycin indicating that dopamine-induced oxidative stress was not involved in the **toxicity** of these compounds. However, flattened cell subvariants of the 1.9 cells, which do not have any neuron-specific characteristics, did not exhibit increased sensitivity to nigericin indicating that some neuronal characteristic of the 1.9 cells contributed to the **toxicity** of nigericin. After the neuronatin-beta gene was transfected into and expressed in the 1.9 cells, they regained wild type PC12 levels of resistance to nigericin, rotenone and valinomycin. These studies suggest that the function of neuronatin during development could be to protect developing cells from toxic insult occurring during that period.

L14 ANSWER 6 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Wessig, J. A. [Reprint Author]; Lewerenz, J. [Reprint Author]; Leypoldt, F. [Reprint Author]; Thomsen, S. [Reprint Author]; Methner, A. [Reprint Author]
TI RESISTANCE TO GLUTAMATE MEDIATED OXIDATIVE STRESS LEADS TO INCREASED mRNA EXPRESSION OF THE HOMEOBOX TRANSCRIPTION FACTOR PEM.
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 486.3. http://sfn.scholarone.com. cd-rom. Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
AB Oxidative stress is involved in the pathogenesis of several neurological disorders including Alzheimers dementia, Parkinsons disease and stroke. It can be studied in the mouse hippocampal cell line Ht22 by adding glutamate to the extracellular space, which leads through inhibition of a cystine/glutamate antiporter to glutathione depletion and consequently to apoptotic cell death by oxidative stress. We selected Ht22 cells resistant to glutamate-mediated cell death to screen for regulated genes possibly modulating susceptibility to oxidative glutamate **toxicity** . Regulated transcripts were identified by subtractive suppression hybridisation and northern blotting. This revealed prominent upregulation of several gene transcripts including Placental/Embryonal Early Gene (PEM). This homeobox transcription factor has not been implicated in oxidative stress or programmed cell death before. Here we show the effects of overexpression of PEM on programmed cell death in transiently transfected Ht22 cells, tet-inducible HEK293 cells and SFV-transduced rat primary cortical cultures.

L14 ANSWER 7 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Guerri, Consuelo [Reprint author]; Pascual, Maria; Renau-Piqueras, Jaime
TI Glia and fetal alcohol syndrome.
SO Neurotoxicology (Little Rock), (October, 2001) Vol. 22, No. 5, pp. 593-599. print.
CODEN: NRTXDN. ISSN: 0161-813X.
AB Glial cells and their interactions with neurons play vital roles during the ontogeny of the nervous system and in the adult brain. Alcohol intake during pregnancy can cause mental retardation and neurobehavioral disorders as well as fetal alcohol syndrome (FAS). Clinical and experimental evidence indicate that in utero alcohol exposure induces structural and functional abnormalities in gliogenesis and in glial-neuronal interactions, suggesting a potential role of glial cells on ethanol-induced developmental brain abnormalities. In vivo studies have shown ethanol-associated alterations in the migration of neurons and radial glial as well as in astrogliogenesis and myelin development. In astrocytes in primary culture, ethanol has been found to (1) impair cell growth and differentiation, (2) decrease the levels of glial fibrillary acidic protein or GFAP (an astrocyte marker) and its **gene expression** and (3) interfere with the stimulatory effect of trophic factors affecting their release and receptor expression. Evidence

also suggests that ethanol affects intracellular protein trafficking, which may mediate some effects of ethanol on astroglial cells. These findings suggest that glial cells are target of ethanol **toxicity** during brain development and may underlie the neurodevelopmental abnormalities observed after in utero alcohol exposure and in FAS.

L14 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Kovacs, Atilla D.; Cebers, Gvido; Cebere, Aleta; Moreira, Tiago; Liljequist, Sture [Reprint author]
TI Cortical and striatal neuronal cultures of the same embryonic origin show intrinsic differences in glutamate receptor expression and vulnerability to excitotoxicity.
SO Experimental Neurology, (March, 2001) Vol. 168, No. 1, pp. 47-62. print. CODEN: EXNEAC. ISSN: 0014-4886.
AB Cortical and striatal cultures were prepared from the same embryonic rat brains and maintained in identical culture conditions. In this way, the intrinsic, genetically imprinted differences determine the responses of cortical and striatal neurons in comparative studies. Cortical and striatal neurons differed in their sensitivity to glutamate receptor-mediated neurotoxicity as measured by the MTT cell viability assay. On the 8th day in vitro, striatal cultures were less sensitive to N-methyl-D-aspartate (NMDA)-induced **toxicity** than cortical, although both cultures were equally vulnerable to alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA)- or kainate-induced **toxicity** . The AMPA receptor-mediated cell death in cortical cultures, however, was much more dependent on preventing AMPA receptor desensitization than in striatal cultures. Furthermore, glutamate-induced neurotoxicity was primarily mediated by NMDA receptors in cortical cultures, while blockade of either NMDA or AMPA receptors gave almost complete protection against glutamate in striatal cultures. To elucidate the molecular mechanisms responsible for the observed differences, we analyzed the expression of NMDA receptor subunits (NR1, NR2A-C) at the mRNA and the protein level in cortical and striatal cultures as well as in standard cerebellar granule cell cultures. The lowest expression level of NMDA receptor subunits was found in striatal cultures, thereby providing a possible explanation for their lower sensitivity to NMDA. Remarkable differences were found between the relative rates of mRNA and **protein expression** for NR1 and NR2B in the three cultures, indicative of intrinsic differences in the posttranscriptional regulation of NMDA receptor subunit expression in cultures from various brain regions.

L14 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
IN Snodgrass, H. Ralph
TI **Toxicity** typing using **embryoid bodies**
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
AB This invention provides methods and systems for identifying and typing **toxicity** of chem. compns., as well as for screening new compns. for **toxicity**. The invention involves detecting alterations in **gene** or **protein expression** and hence establishing **mol. profiles** in isolated mammalian **embryoid bodies** contacted with various chem. compns. of known and unknown **toxicities**, and correlating the **mol. profiles** with **toxicities** of the chem. compns.

L14 ANSWER 10 OF 24 MEDLINE on STN
AU Trillo-Pazos G; McFarlane-Abdulla E; Campbell I C; Pilkington G J; Everall I P
TI Recombinant nef HIV-IIIB protein is toxic to human neurons in culture.
SO BRAIN RESEARCH, (2000 May 12) 864 (2) 315-26.
Journal code: 0045503. ISSN: 0006-8993.
AB The expression of HIV-1 negative factor (nef) has been positively correlated with HIV disease progression [Z. Hanna, D.G. Kay, N. Rebai, A. Guimond, S. Jothy, P. Jocicoeur, Nef harbors a makor determinant of

pathogenicity for an AIDS-like disease induced by HIV-1 in transgenic mice. Cell 95 (1998) 163-175]. Nef expression has been detected in HIV infected human brains with neuronal damage [A. Ranki, M. Nyberg, V. Ovod, M. Haltia, I. Elovaara, R. Raininko, H. Haapsalo, K. Krohn, Abundant **expression** of HIV Nef and Rev **proteins** in brain astrocytes in associated with dementia, AIDS 9(9) (1995) 1001-1008; Y. Saito, L.R. Sharer, M.G. Epstein, J. Michaels, M. Mintz, M. Londer, K. Golding, B.M. Blumberg, Overexpression of nef as a marker for restricted HIV-1 infection of astrocytes in postmorten paediatric central tissues, Neurology 14 (1994) 474-480]. It is postulated that nef may contribute to the neuronal damage observed in the brain of those with late HIV disease. To test this, the potential **toxicity** of recombinant nef (from HIV-1 IIIB) was compared to the **neurotoxin** human tumour necrosis alpha (TNFalpha) on human brain cells in culture. SK-N-SH neuroblastoma, primary human neurons and glial cells were exposed to recombinant nef or TNFalpha protein for 3 days or twice over 6 days. Cell viability was assessed by Trypan Blue, lactate dehydrogenase (LDH) release and MTT assays. Nuclear fragmentation was detected using the Hoechst Blue nuclear dye assay. Both nef and TNFalpha (100 ng/ml) caused a significant 30% reduction of SK-N-SH cell numbers after 3 days exposure (P=0. 001). At this time, exposure to nef caused evident fragmented nuclei in these cultures. Human neuronal cultures had a 32 and 33% decrease in cell number after 6 days exposure to either nef or TNFalpha, respectively (P<0.001). Furthermore, as previously shown [J. He, C.M. DeCastro, G.R. Vandenbark, J. Busciglio, D. Gabuzda, Astrocyte apoptosis induced by HIV-1 transactivation of the c-kit protoonocogene, Proc. Natl. Acad. Sci. 94 (1997) 3954-3959], a 3-day exposure to nef significantly reduced human glial cell number by 25% (P=0.001). Recombinant nef and TNFalpha compromise human neurons in culture. Thus, like other virotoxins, it is shown for the first time that nef may also contribute to neuronal damage that has been reported in dementia in late HIV disease.

L14 ANSWER 11 OF 24 MEDLINE on STN
AU Llansola M; Minana M D; Montoliu C; Saez R; Corbalan R; Manzo L; Felipo V
TI Prenatal exposure to aluminum reduces expression of neuronal nitric oxide synthase and of soluble guanylate cyclase and impairs glutamatergic neurotransmission in rat cerebellum.
SO JOURNAL OF NEUROCHEMISTRY, (1999 Aug) 73 (2) 712-8.
Journal code: 2985190R. ISSN: 0022-3042.
AB Exposure to aluminum (Al) produces neurotoxic effects in humans. However, the molecular mechanism of Al neurotoxicity remains unknown. Al interferes with glutamatergic neurotransmission and impairs the neuronal glutamate-nitric oxide-cyclic GMP (cGMP) pathway, especially in rats prenatally exposed to Al. The aim of this work was to assess whether Al interferes with processes associated with activation of NMDA receptors and to study the molecular basis for the Al-induced impairment of the glutamate-nitric oxide-cGMP pathway. We used primary cultures of cerebellar neurons prepared from control rats or from rats prenatally exposed to Al. Prenatal exposure to Al prevented glutamate-induced proteolysis of the microtubule-associated protein-2, disaggregation of microtubules, and neuronal death, indicating an impairment of NMDA receptor-associated signal transduction pathways. Prenatal exposure to Al reduced significantly the content of nitric oxide synthase and guanylate cyclase and increased the content of calmodulin both in cultured neurons and in the whole cerebellum. This effect was selective for proteins of the glutamate-nitric oxide-cGMP pathway as the content of mitogen-activated protein kinase and the synthesis of most proteins were not affected by prenatal exposure to Al. The alterations in the **expression** of **proteins** of the glutamate-nitric oxide-cGMP pathway could be responsible for some of the neurotoxic effects of Al.

L14 ANSWER 12 OF 24 MEDLINE on STN

AU Petersen A; Brundin P
TI Effects of ciliary neurotrophic factor on excitotoxicity and calcium-ionophore A23187-induced cell death in cultured embryonic striatal neurons.
SO EXPERIMENTAL NEUROLOGY, (1999 Dec) 160 (2) 402-12.
Journal code: 0370712. ISSN: 0014-4886.
AB Ciliary neurotrophic factor (CNTF) has a protective effect on the striatum in animal models of Huntington's disease. However, the mechanism through which it exerts its effect is not clear. In this study, we show that there is a concentration-dependent direct protective effect of CNTF against N-methyl-D-aspartate-mediated excitotoxicity on striatal neurons in vitro. The CNTF has to be added more than half an hour before the insult for the effect to occur and its effect is eliminated by the presence of the protein synthesis inhibitor cycloheximide. This suggests that the protective mechanism of CNTF does not involve acute interference with the glutamate receptors, but probably requires **gene/protein expression**. We have also shown that the effect of CNTF against glutamate-induced excitotoxicity is dependent on the concentration of glutamate with a protective effect more evident at a low grade excitotoxic insult. Finally, we saw no effect of CNTF on calcium ionophore A23187-induced **toxicity** in striatal cultures, indicating that the growth factor does not promote survival by enhancing general defenses against raised intracellular levels of calcium.

L14 ANSWER 13 OF 24 MEDLINE on STN
AU Takashima H; Tsujihata M; Kishikawa M; Freed W J
TI Bromocriptine protects dopaminergic neurons from levodopa-induced **toxicity** by stimulating D(2)receptors.
SO EXPERIMENTAL NEUROLOGY, (1999 Sep) 159 (1) 98-104.
Journal code: 0370712. ISSN: 0014-4886.
AB Neuroprotective properties of bromocriptine, a D(2) receptor agonist, were investigated using the in vitro neurotoxicity of levodopa for dopaminergic neurons from rat embryonic ventral mesencephalon. Levodopa, when added to the culture medium, showed **toxicity** which was specific for dopaminergic neurons. Bromocriptine was found to protect dopaminergic neurons from levodopa **toxicity**. Another D(2) agonist, 2-(N-phenethyl-N-propyl-amino-5-hydroxytetralin, showed similar protective effects. The neuroprotective effect of bromocriptine was inhibited by supplementation of the culture medium with sulpiride, a D(2) antagonist, or by D(2) receptor knockdown with an antisense oligonucleotide. Dopaminergic neurons treated with levodopa showed an increase in free radicals. These data suggest that neuroprotective properties of bromocriptine seen in this cellular model of neurotoxicity are dependent on dopamine D(2) autoreceptor binding and that levodopa **toxicity** may be related to increased free radical generation in dopaminergic neurons.

L14 ANSWER 14 OF 24 MEDLINE on STN
AU Meucci O; Fatatis A; Simen A A; Bushell T J; Gray P W; Miller R J
TI Chemokines regulate hippocampal neuronal signaling and gp120 neurotoxicity.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Nov 24) 95 (24) 14500-5.
Journal code: 7505876. ISSN: 0027-8424.
AB The HIV-1 envelope protein gp120 induces apoptosis in hippocampal neurons. Because chemokine receptors act as cellular receptors for HIV-1, we examined rat hippocampal neurons for the presence of functional chemokine receptors. Fura-2-based Ca imaging showed that numerous chemokines, including SDF-1alpha, RANTES, and fractalkine, affect neuronal Ca signaling, suggesting that hippocampal neurons possess a wide variety of chemokine receptors. Chemokines also blocked the frequency of spontaneous glutamatergic excitatory postsynaptic currents recorded from these neurons and reduced voltage-dependent Ca currents in the same neurons. Reverse

transcription-PCR demonstrated the expression of CCR1, CCR4, CCR5, CCR9/10, CXCR2, CXCR4, and CX3CR1, as well as the chemokine fractalkine in these neurons. Both fractalkine and macrophage-derived chemokine (MDC) produced a time-dependent activation of extracellular response kinases (ERK)-1/2, whereas no activation of c-JUN NH2-terminal protein kinase (JNK)/stress-activated protein kinase, or p38 was evident. Furthermore, these two chemokines, as well as SDF-1alpha, activated the Ca- and cAMP-dependent transcription factor CREB. Several chemokines were able also to block gp120-induced apoptosis of hippocampal neurons, both in the presence and absence of the glial feeder layer. These data suggest that chemokine receptors may directly mediate gp120 neurotoxicity.

L14 ANSWER 15 OF 24 MEDLINE on STN
AU Seidel B; Keilhoff G; Reinheckel T; Wolf G
TI Differentially expressed genes in hippocampal cell cultures in response to an excitotoxic insult by quinolinic acid.
SO BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1998 Oct 1) 60 (2) 296-300. Journal code: 8908640. ISSN: 0169-328X.
AB The NMDA-type glutamate receptor agonist quinolinic acid (QA), which causes tissue lesions in the rat brain as well as cell loss in neuronal cultures, is widely used in models of glutamate excitotoxicity. The aim of this study was to evaluate the alterations in **gene expression** in a primary hippocampal cell culture after exposure to QA. By means of differential mRNA display, we were able to pinpoint as many as 23 bands which appeared to be upregulated after a 6-h treatment with quinolinic acid. The differential expression of 13 cDNAs could be confirmed by dot blot and/or Northern analysis. Of the cDNAs, the p112 regulatory subunit of the 26S proteasome, a PDGF-associated protein and the glia-derived protease nexin PN-1 could be identified. The results provide emphasis to the participation of proteolysis and protease inhibition in neurodegenerative processes.

L14 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Bales, Kelly R.; Du, Yansheng; Dodel, Richard C.; Yan, Guang-Mei; Hamilton-Byrd, Elizabeth; Paul, Steven M. [Reprint author]
TI The NF-kappaB/Rel family of proteins mediates A beta-induced neurotoxicity and glial activation.
SO Molecular Brain Research, (June 1, 1998) Vol. 57, No. 1, pp. 63-72. print. CODEN: MBREE4. ISSN: 0169-328X.
AB The beta-amyloid peptide (Abeta) is deposited in neuritic plaques which are characteristic features of Alzheimer's disease (AD). Prominent neurodegeneration and glial activation occurs around these plaques leading to the hypothesis that Abeta may play a causative role in the neuronal loss and the inflammatory response associated with AD. Here we show that Abeta-induced **toxicity** of cultured fetal rat cortical neurons is associated with internucleosomal DNA fragmentation beginning just 6 h after neurons are exposed to Abeta. Additionally, constitutive NF-kappaB activity readily measured in fetal rat cortical neurons decreases in a concentration- and time-dependent fashion following exposure to Abeta, but there is no corresponding decrease in NF-kappaB mRNA or protein (p65). An upregulation of both IkappaBalpha protein and mRNA which occurs in cortical neurons exposed to Abeta may be responsible for retaining NF-kappaB in the cytoplasm accounting for the observed decrease in activated NF-kappaB. The latter is supported by the observation that pretreatment of cortical cultures with an antisense oligonucleotide to IkappaBalpha mRNA is neuroprotective. In contrast to cortical neurons, exposure of rat primary astroglial cultures to Abeta results in a concentration- and time-dependent activation of NF-kappaB with subsequent upregulation of IL-1beta and IL-6. Our data suggest that A beta-induced neurotoxicity as well as astrocyte activation may be medicated by the NF-kappaB/Rel family of proteins, and thus alterations in NF-kappaB-directed **gene expression** may contribute to both the neurodegeneration and inflammatory response which occur in AD.

L14 ANSWER 17 OF 24 MEDLINE on STN
AU Samdani A F; Newcamp C; Resink A; Facchinetti F; Hoffman B E; Dawson V L; Dawson T M
TI Differential susceptibility to neurotoxicity mediated by neurotrophins and neuronal nitric oxide synthase.
SO JOURNAL OF NEUROSCIENCE, (1997 Jun 15) 17 (12) 4633-41.
Journal code: 8102140. ISSN: 0270-6474.
AB NMDA neurotoxicity, which is mediated, in part, by formation of nitric oxide (NO) via activation of neuronal NO synthase (nNOS), is modulated by neurotrophins. nNOS expression in rat and mouse primary neuronal cultures grown on a glial feeder layer is significantly less than that of neurons grown on a polyornithine (Poly-O) matrix. Neurotrophins markedly increase the number of nNOS neurons, nNOS protein, and NOS catalytic activity and enhance NMDA neurotoxicity via NO-dependent mechanisms when neurons are grown on glial feeder layers. In contrast, when rat or mouse primary cortical neurons are grown on a Poly-O matrix, neurotrophins have no influence on nNOS neuronal number or NOS catalytic activity and reduce NMDA neurotoxicity. Primary neuronal cultures from mice lacking nNOS grown on a glial feeder layer fail to respond to neurotrophin-mediated enhancement of neurotoxicity. Together, these results indicate that nNOS expression and NMDA NO-mediated neurotoxicity are dependent, in part, on the culture paradigm, and neurotrophins regulate the susceptibility to NMDA neurotoxicity via modulation of nNOS. Furthermore, these results support the idea that NMDA neurotoxicity in culture is critically dependent on the developmental state of the neurons being assessed and suggest that, when cortical neurons are cultured on a glial feeder layer, they do not reach nearly as mature a phenotype as when grown on a Poly-O matrix.

L14 ANSWER 18 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AU Valles, S.; Pitarch, J.; Renau-Piqueras, J.; Guerri, C. [Reprint author]
TI Ethanol exposure affects glial fibrillary acidic **protein gene expression** and transcription during rat brain development.
SO Journal of Neurochemistry, (Dec., 1997) Vol. 69, No. 6, pp. 2484-2493. print.
CODEN: JONRA9. ISSN: 0022-3042.
AB Exposure to ethanol during fetal development reduces the astroglial-specific marker glial fibrillary acidic protein (GFAP) and its mRNA levels in brains of fetal rats and in radial glia in primary culture, affecting the proliferation and differentiation of astrocytes. The objectives of this study were to evaluate the possible effect of ethanol on GFAP mRNA levels in astrocytes and to investigate the molecular mechanism(s) involved in ethanol-induced changes in GFAP expression by analyzing the GFAP transcription rate, GFAP mRNA stability, and GFAP DNA methylation. We show here that prenatal exposure to ethanol reduces significantly GFAP immunoreactivity and its mRNA levels in both astrocytes in primary culture and brains of pups from alcohol-fed mothers. Runoff experiments from nuclei of astrocytes indicate that ethanol exposure decreases GFAP transcription rate significantly and reduces GFAP mRNA stability slightly. DNA methylation analysis indicates that prenatal ethanol exposure induces a hypermethylated state of the GFAP DNA in fetal brains. Methylation-mediated repression of GFAP transcription could be a mechanism involved in ethanol-induced reduction of GFAP expression. Ethanol-induced alterations in GFAP expression and astroglial development may underlie the CNS dysfunctions observed after prenatal alcohol exposure.

L14 ANSWER 19 OF 24 MEDLINE on STN
AU Williamson L C; Halpern J L; Montecucco C; Brown J E; Neale E A
TI Clostridial **neurotoxins** and substrate proteolysis in intact neurons: botulinum **neurotoxin** C acts on synaptosomal-associated protein of 25 kDa.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Mar 29) 271 (13) 7694-9.
Journal code: 2985121R. ISSN: 0021-9258.

AB Clostridial **neurotoxins** are zinc endopeptidases that block neurotransmission and have been shown to cleave, in vitro, specific proteins involved in synaptic vesicle docking and/or fusion. We have used immunohistochemistry and immunoblotting to demonstrate alterations in toxin substrates in intact neurons under conditions of toxin-induced blockade of neurotransmitter release. Vesicle-associated membrane protein, which colocalizes with synaptophysin, is not detectable in tetanus toxin-blocked cultures. Syntaxin, also concentrated in synaptic sites, is cleaved by botulinum **neurotoxin** C. Similarly, the carboxyl terminus of the synaptosomal-associated protein of 25 kDa (SNAP-25) is not detectable in botulinum **neurotoxin** A-treated cultures. Unexpectedly, tetanus toxin exposure causes an increase in SNAP-25 immunofluorescence, reflecting increased accessibility of antibodies to antigenic sites rather than increased **expression** of the **protein**. Furthermore, botulinum **neurotoxin** C causes a marked loss of the carboxyl terminus of SNAP-25 when the toxin is added to living cultures, whereas it has no action on SNAP-25 in vitro preparations. This study is the first to demonstrate in functioning neurons that the physiologic response to these toxins is correlated with the proteolysis of their respective substrates. Furthermore, the data demonstrate that botulinum **neurotoxin** C, in addition to cleaving syntaxin, exerts a secondary effect on SNAP-25.

L14 ANSWER 20 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AU Valles, S.; Sancho-Tello, M.; Minana, R.; Climent, E.; Renau-Piqueras, J.; Guerri, C. [Reprint author]

TI Glial fibrillary acid **protein expression** in rat brain and in radial glia culture is delayed by prenatal ethanol exposure.

SO Journal of Neurochemistry, (1996) Vol. 67, No. 6, pp. 2425-2433.
CODEN: JONRA9. ISSN: 0022-3042.

AB The alterations in astrocyte proliferation and differentiation induced by prenatal exposure to alcohol (PEA) suggest that ethanol exposure affects the radial glial cells, the main astrocytic precursors. We have investigated the effects of ethanol on the early stages of astrogliogenesis by analyzing the developmental pattern of vimentin and glial fibrillary acidic protein (GFAP) immunoreactivity and their mRNA levels during embryonic/fetal brain development and in radial glia in primary culture. GFAP appeared late in gestation and at day 5 of culture of radial glia, whereas GFAP mRNA was first detected on fetal day 15 and increased in content on fetal day 21. In contrast, the levels of vimentin and its mRNA were high at fetal day 15 but decreased on day 21. Alcohol exposure delays the appearance of GFAP and its mRNA and significantly decreases the GFAP expression in fetal brain and in primary culture of radial glia. In addition, some morphological alterations were observed in PEA glial cells in culture. These results demonstrate that astroglial precursor cells are damaged by prenatal exposure to ethanol and suggest that abnormalities in the astrogliogenesis may underlie the disruption in neuronal migration and other CNS alterations observed after prenatal ethanol exposure.

L14 ANSWER 21 OF 24 MEDLINE on STN

AU Prehn J H; Bindokas V P; Jordan J; Galindo M F; Ghadge G D; Roos R P; Boise L H; Thompson C B; Krajewski S; Reed J C; Miller R J

TI Protective effect of transforming growth factor-beta 1 on beta-amyloid neurotoxicity in rat hippocampal neurons.

SO MOLECULAR PHARMACOLOGY, (1996 Feb) 49 (2) 319-28.
Journal code: 0035623. ISSN: 0026-895X.

AB Neurodegeneration associated with Alzheimer's disease is believed to involve **toxicity** to beta-amyloid (A beta) and related peptides. Treatment of cultured rat hippocampal neurons with A beta 1-40 (1 microM) or the active fragment A beta 25-35 (1 microM) for 5 days led to a approximately 40-50% decrease in neuronal viability. The hydrophilic

antioxidant ascorbic acid (300 microM) and the lipophilic antioxidant 2-mercaptoethanol (10 microM) both protected significantly against A beta neurotoxicity. Despite the protective effects of these antioxidants, both acute and chronic treatments with A beta 25-35 did not increase production of superoxide anions, as monitored with the fluorescent probe hydroethidine. Similarly, overexpression of Cu/Zn-superoxide dismutase using adenovirus-mediated gene transfer did not protect against A beta neurotoxicity. A beta neurotoxicity, however, was prevented in cultures infected with a recombinant, replication-defective adenovirus overexpressing the Ca2+ binding protein calbindin D28k. Transforming growth factor-beta 1 (TGF-beta 1) has been shown to protect neurons against both Ca(2+)- and free radical-mediated neuronal degeneration. We found that A beta neurotoxicity was significantly attenuated by single treatments with TGF-beta 1 (0.1-10 ng/ml) and prevented by repetitive treatments (10 ng/ml/day). The protective effects of TGF-beta 1 were associated with a preservation of mitochondrial potential and function, as determined with rhodamine-123-based microfluorimetry. Because both increased oxidative stress and pathophysiological Ca2+ fluxes can impair mitochondrial function, preservation of mitochondrial potential by TGF-beta 1 could be directly associated with its protection against A beta neurotoxicity. The ability of TGF-beta 1 to increase the **expression** of the anti-apoptotic **proteins** Bcl-2 and Bcl-XL is discussed in this context.

L14 ANSWER 22 OF 24 MEDLINE on STN
AU Forloni G; Bugiani O; Tagliavini F; Salmona M
TI Apoptosis-mediated neurotoxicity induced by beta-amyloid and PrP fragments.
SO MOLECULAR AND CHEMICAL NEUROPATHOLOGY, (1996 May-Aug) 28 (1-3) 163-71. Journal code: 8910358. ISSN: 1044-7393.
AB The neurotoxic activity of beta-amyloid (beta A) and prion protein (PrP) fragments contributed to the hypothesis concerning a causal role of amyloid deposits in Alzheimer disease (AD) and in prion-related encephalopathies. In this study, we investigated some aspects of the molecular mechanisms associated with neurotoxic activity of synthetic peptides homologous to beta A (beta 25-35) or PrP (PrP106-126) fragments. Chronic (5-7 d) exposure to both peptides induced neuronal death by apoptosis, as suggested by biochemical and morphological analysis. The apoptotic mechanism was confirmed by ultrastructural examination. The intracellular cascade of events activated by peptides was investigated by Northern blot and PCR analysis of **expression** of early **genes** (c-fos, c-jun, c-myc) and other proteins (p53, SGP-2 bcl-2, HSP70, Ich-1) potentially involved in apoptosis. With the exception of bcl-2 mRNA decrease and a slight increase of SGP-2 in PrP106-126-treated cells, no consistent alterations of these mRNA expressions were found in neuronal cells exposed to beta 25-35 or PrP106-126. Furthermore, we synthesized amidated homologs of both peptides with low amyloidogenic activity to test directly the relationship between amyloid fibrils and cell death. The neurotoxicity exhibited by PrP106-126-NH2 was similar to that observed with original peptide, whereas the amidation of beta 25-35 partially reduced the neurotoxicity of this peptide.

L14 ANSWER 23 OF 24 MEDLINE on STN
AU Cheng B; Christakos S; Mattson M P
TI Tumor necrosis factors protect neurons against metabolic-excitotoxic insults and promote maintenance of calcium homeostasis.
SO NEURON, (1994 Jan) 12 (1) 139-53. Journal code: 8809320. ISSN: 0896-6273.
AB Emerging data indicate that neurotrophic factors and cytokines utilize similar signal transduction mechanisms. Although neurotrophic factors can protect CNS neurons against a variety of insults, the role of cytokines in the injury response is unclear. We now report that TNF beta and TNF alpha (1-100 ng/ml) can protect cultured embryonic rat hippocampal, septal, and cortical neurons against glucose deprivation-induced injury and excitatory

amino acid **toxicity**. The elevation of intracellular calcium concentration ([Ca2+]i) induced by glucose deprivation, glutamate, NMDA, or AMPA was attenuated in neurons pretreated with TNF beta. The mechanism whereby TNFs stabilize [Ca2+]i may involve regulation of the **expression** of **proteins** involved in maintaining [Ca2+]i homeostasis, since both TNF beta and TNF alpha caused a 4- to 8-fold increase in the number of neurons expressing the calcium-binding protein calbindin-D28k. These data suggest a neuroprotective role for TNFs in the brain's response to injury.

L14 ANSWER 24 OF 24 MEDLINE on STN
AU Mattson M P; Kumar K N; Wang H; Cheng B; Michaelis E K
TI Basic FGF regulates the expression of a functional 71 kDa NMDA receptor protein that mediates calcium influx and neurotoxicity in hippocampal neurons.
SO JOURNAL OF NEUROSCIENCE, (1993 Nov) 13 (11) 4575-88.
Journal code: 8102140. ISSN: 0270-6474.
AB Basic fibroblast growth factor (bFGF) was recently found to modulate the outgrowth-regulating effects of glutamate, and protected neurons from several brain regions against excitotoxi/ischemic damage. We provide evidence that the excitoprotective mechanism of bFGF involves suppression of the expression of a 71 kDa NMDA receptor protein (NMDARP-71). NMDARP-71 protein and mRNA levels were reduced in neurons in bFGF-treated hippocampal cell cultures. The levels of the NMDARP-71 were not reduced by NGF or epidermal growth factor, and bFGF did not reduce the level of mRNA for the GluR1 kainate/AMPA receptor, demonstrating the specificity of the effect of bFGF on the NMDARP-71. The reduction in NMDARP-71 expression in bFGF-treated neurons was correlated with reduced vulnerability to NMDA neurotoxicity. A major role for NMDARP-71 in calcium responses to NMDA and excitotoxicity was demonstrated using antisense oligonucleotides directed against NMDARP-71. Northern and Western blot analysis and immunocytochemistry showed that NMDARP-71 antisense oligonucleotides caused a selective suppression of NMDARP-71 mRNA and protein levels during 12-44 hr exposure periods. Elevations in intracellular calcium levels normally caused by glutamate and NMDA were attenuated in neurons exposed to NMDARP-71 antisense oligonucleotide; calcium responses to kainate were relatively unaffected. NMDARP-71 antisense oligonucleotides protected the neurons against excitotoxicity. Thus, NMDARP-71 is a necessary component of an NMDA receptor mediating calcium responses and neurotoxicity in hippocampal neurons. Taken together, these data identify a mechanism whereby bFGF can modify neuronal responses to glutamate, and suggest that regulating the expression of excitatory amino acid receptors may provide a means for growth factors to influence the plasticity and degeneration of neural circuits.

=>